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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER
MOORE, WILLIAM W

ART UNIT	PAPER NUMBER
1652	12

DATE MAILED: 01/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,198	JENSENIUS ET AL.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,22,28 and 40-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *46* is/are allowed.

6)☒ Claim(s) *1-10, 22, 28, and 46- 56* is/are rejected.

7)☒ Claim(s) *11 and 41-45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election **with** traverse of Group I, claims 1-11 and 22 in Paper No. 10, filed November 7, 2002, is acknowledged. The new claims 40-56 that, together with amendments to claims 4-6 and 8-11 submitted with Applicant's Amendment B, Paper No. 11 filed November 7, 2002, correspond to the elected subject matter of Group I. Applicant's traversal on the grounds that the subject matter of claim 28 – the only claim in Group II – depends from claim 1 and therefore may properly be joined with claim 1 and examined together with the claim is persuasive, the restriction requirement between Groups I and II is RESCINDED and claims 1-11, 22, 28 and 40-56 are examined herein.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 9, 10, 22, 28 and 56 are rejected under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

The subject matters of claims 9, 10, 22, 28 and 56 elected for prosecution herein are neither disclosed by the present specification nor enabled by the prior art made of record herewith. While a polypeptide product, and a method of treatment, described by these might have had a specific and a substantial utility if it existed, or had been enabled at the time the instant specification filed, there is no disclosure in the specification of any serine protease inhibitory product that shares a portion of, or that is related to, the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2, thus there is no credible utility disclosed. Similarly, no credible utility disclosed where there is no disclosure in the specification of a method for treating any specific disease state or medical condition with any product that shares a portion of, or that is related to, the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2, nor any suggestion as to how such a method might be accomplished.

Mere allegations of a prospective, potential, utility cannot rise to the level of a credible assertion of a specific *in vitro* or *in vivo* utility that is substantial. Indeed, the specification's lack of disclosure thereof indicates the contrary: That Applicant knew of no product that would permit an immediate use by the public of an undisclosed product and that Applicant knew of no treatment method with a disclosed product. Applicant is invited to establish that credible utilities existed for the undisclosed product and undisclosed method.

No rejection of claims 1-3, 7, 8, 11, 46, 47, and 49-55 elected for prosecution herein is stated under 35 U.S.C. §101 because each of these claims embraces at least one embodiment of a human MASP-2 polypeptide demonstrated in Example 7 and Figure 4 of the specification to be capable of the specific activation of the human complement component C4, an invention which possesses a specific, substantial and demonstrable *in vitro* utility. No rejection of claims 4-6, 40-45, 48 and 54 elected for prosecution herein is stated under 35 U.S.C. §101 because each of these claims embraces a peptide component of human MASP-2 polypeptide which may be used to raise antisera that may specifically recognize and detect a MBL/MASP-2 complex, which peptide is an invention which possesses a specific, substantial and credible *in vitro* utility.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 10, 22, 28 and 56 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-10, 22, 28, and 47-56 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such

a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to exemplify or describe the preparation of the subject matters of any serine protease inhibitory product that shares a portion of, or that is related to, the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2, and fails to exemplify the preparation of a pharmaceutical composition of claim 22 or the practice of a method of treatment of claim 28. Neither does the specification anywhere exemplify or describe the preparation of any of the, generic, divergent proteases or polypeptide products of claims 1-4, 7 and 47-55 where the specification contemplates - see page 28, lines 8-19, with respect to generic claims 1-8 - divergent products that may exceed the percentage identity recitations embodied in claims 47-55. Where the artisan reading the specification cannot ascertain the nature of a claimed, but undisclosed, inhibitory product of claims 9, 10 and 56, the artisan could not recognize that Applicant was in possession of these subject matters at the time the specification was filed. The rejected claims 47-54 reach generic proteins that differ at as much as 1% of the positions in the 671-amino acid sequence of SEQ ID NO:2, at as much as 15% of the positions of its included 41-amino acid sequence of SEQ ID NO:1, but neither the claims nor the specification describe where the differences occur, nor what the differences might be, and the specification does not otherwise disclose or suggest the nature or source of any of the generic proteins that meet the limitations of the claims. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). The specification furnishes no relevant identifying characteristics of a protease that diverges at as many as 6 amino acid positions from the sequence of SEQ ID NO:2, or of a peptide product that diverges at as many as 6 amino acid positions from the sequence of SEQ ID

NO:1, neither does it provide any characteristic permitting correlation between undisclosed structures of any protein product among the myriad species of generic proteins of claims 47-54 and the disclosed amino acid sequences of SEQ IDs NOs:1 and 2.

The Court of Appeals for the Federal Circuit held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Indeed, claims 47-54 rejected herein are, like the claims invalidated by the appellate panel in *University of California v. Eli Lilly*, designed to embrace other, as yet unknown, mammalian proteases. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of any of these undisclosed generic proteins to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant fields of molecular biology and medicine could not predict the structure, or other properties, of the generic proteases of claims 1, 4, 7 and 47-55, the nature of any inhibitors of claims 9, 10 and 56, or the nature of the pharmaceutical composition and treatment method of claims 22 and 28.

Claims 1-10, 22, 28, and 47-56 are rejected under 35 U.S.C. §112, first paragraph, because the specification is not enabling for any embodiment of an inhibitory product, for any embodiment of a method of treatment using a disclosed protease, nor for the preparation of a functioning human MASP-2 protease having an amino acid sequence that diverges from the amino acid sequence of SEQ ID NO:2, nor for a product that diverges as much as 15% from the amino acid sequence of SEQ ID NO:1 that has any use in identifying a native, human, MBL-MASP-2 complex. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and use the invention commensurate in scope with these claims.

Claims 9, 10, 22, 28, and 56 are not enabled because there is no disclosure of any product that might have an inhibitory activity of products of claims 9, 10 and 56, nor any suggestion as to where such a product might be found, and because there is no disclosure of the preparation of an effective pharmaceutical composition comprising a disclosed product, nor any method of use of a disclosed product in treating any recognizable medical condition from which a patient might suffer. Claims 1-7, and 47-55 are not enabled because they contemplate - see page 28, lines 8-19, with respect to the generic claims 1-7 - arbitrary assignments of any or all of amino acid substitutions, additions or deletions in the sequence of the disclosed, native, human MASP-2 protease of SEQ ID NO:2 at as many as 6 of the amino acid positions and because they contemplate arbitrary assignments of any or all of amino acid substitutions, additions or deletions in the sequence of the disclosed, native, human MASP-2 protease amino-terminal peptide at many as 6 of the amino acid positions in its 41-amino acid peptide. This rejection is stated under the first paragraph of the statute because the specification cannot support introduction of at least 6 amino acid alterations, in the amino acid sequence of SEQ ID NO:2, nor the introduction 6 alterations in the amino acid sequences of SEQ ID NO:1 that will permit its use in raising MASP-2 recognizing antibodies, where the alterations are amino acid insertions, deletions, or substitutions anywhere, in any combination or any pattern, in the amino acid sequences set forth in SEQ ID NOs:1 and 2. Indeed, Applicant's specification cannot identify six amino acids in the primary sequence of human MASP-2-related proteases – such as the prior art MASP-1, C1 and C1q – that might be altered, nor teach the nature of an alteration that may be made, which permits a resulting polypeptide to function as a protease. Mere sequence perturbation cannot enable the design and preparation of nucleotide sequences encoding a myriad of divergent protease enzymes and provide the public with a nucleotide sequence encoding an enzyme that retains its native function. This

is well demonstrated by the publication of Seffernick et al., 2001, Journal of Biochemistry, Vol. 183, pages 2405-2410, made of record herewith, who teach that the alteration of 9 amino acids in a sequence of 475 amino acids, a scant 2% of the native amino acid positions, in a deaminase will suffice to alter its substrate specificity and require it to catalyze different reactions even though, p. 2409, these alterations do not at all alter its tertiary structure and are spread throughout its primary structure.

It is well settled that 35 U.S.C. §112, first paragraph, requires that a disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors relevant to analysis of enablement). The standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); see also, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The Federal Circuit approved the standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997).

The Federal Circuit has also considered whether definitional statements might enable a claim scope argued to extend beyond a disclosed gene product having its native amino acid

sequence to embrace a specific variant gene product encoded by a specifically-altered DNA sequence. *Genentech, Inc. v. The Wellcome Found. Ltd.*, 29 F.3d 1555, 31 USPQ2d 1161 (Fed. Cir. 1994). The court held that only a narrow structural and functional definition was enabling precisely because the sweeping definitions of scope in the patent specification could not reasonably have been relied upon by the PTO in issuing the patent. *Genentech*, 29 F.3d 15 at 1564-65, 31 USPQ2d at 1168. Applying the "*Forman*" factors discussed in *Wands, supra*, to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering the amino acid sequences of products of SEQ IDs NOs:1 and 2 to the extent recited in the claims,

b) the specification lacks working examples wherein products of SEQ IDs NOs:1 and 2 are altered to the extent recited in the claims,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no members of the class of human products having amino acid sequences related to SEQ IDs NOs:1 and 2 have had as many as six amino acids specifically identified for concurrent modification.

Thus the scope of subject matters embraced by claims 1-7, 9, 10, 22, 28, and 47-56 is unsupported by the present specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 40 is rejected under 35 U.S.C. §102(b) as being anticipated by Rasmussen et al., 1996, Journal of Urology, Vol. 155, pages 2113-2119.

Rasmussen et al. disclose a 18.5 kilodalton polypeptide that comprises a sequence of 16 amino acids completely identical to the sequence of 16 amino acids from position 15

through position 30 of SEQ ID NO:1, inclusive, which is, in turn, comprised within SEQ ID NO:2 therein, meeting the limitations of claim 40 herein.

Allowable Subject Matter

Claim 46 is allowed because the publications made of record herewith do not disclose or suggest polypeptides have the amino acid sequences of either SEQ ID NO:1 or SEQ ID NO:2, neither do they indicate that polypeptides having the amino acid sequences of either SEQ ID NO:1 or SEQ ID NO:2 were reported in any prior publication. Claims 11 and 41-45 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached between 9:00AM-5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. Further fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. The examiner's direct FAX telephone number is 703.746.3169. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
January 23, 2003

PONNATHAPURA ACHUTAMURTHY
SUPERVISORY PATENT EXAMINER